ENDOCERVICAL PLACENTAL SITE TROPHOBLASTIC TUMOR: A CASE REPORT

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SUMMARY

Objective: We report the treatment of a patient with persistent gestational trophoblastic disease.

Case Report: A 42-year-old woman, gravida 2, para 1, was initially diagnosed with choriocarcinoma from curettage specimens. She initially responded to aggressive chemotherapy but later was unresponsive. Subsequently, she underwent total abdominal hysterectomy; the resected uterus revealed a placental site trophoblastic tumor. Adjuvant chemotherapy was given. The serum human chorionic gonadotropin level progressively decreased to zero. The patient was alive and well at the time of writing.

Conclusion: Chemotherapy-resistant persistent gestational trophoblastic disease may suggest placental site trophoblastic tumor. Surgery is the main treatment for placental site trophoblastic tumor. [*Taiwanese J Obstet Gynecol* 2004;43(2):120–124]

Key Words: placental site trophoblastic tumor, surgery, chemotherapy

Introduction

Placental site trophoblastic tumor (PSTT) is the rarest type of gestational trophoblastic disease derived from intermediate trophoblasts. Since it was first reported by Kurman et al in 1976 [1], more than 100 cases have been reported in the English literature. As it is infrequently seen, the clinical behavior and pathogenesis of PSTT are still not completely understood. Here, we present a case of PSTT and review the literature for management options.

Case Report

A 42-year-old woman, gravida 2, para 1, presented with irregular genital bleeding for 3 months. She had undergone therapeutic dilatation and curettage (D&C) for a spontaneous abortion in May 2002. Otherwise, the patient was in excellent health. A D&C was performed on May 2, 2003, at another hospital because of irregular genital bleeding. The pathology report interpreted the specimen as a choriocarcinoma. The serum human chorionic gonadotropin (β-hCG) concentration was elevated to 1,798 mIU/mL. She was treated with EMA/CO chemotherapy (etoposide 100 mg/m^2 on days 1 and 2, methotrexate 100 mg/m^2 on day 1 followed immediately by a 12-hour infusion of 200 mg/m^2 methotrexate with leukovorin rescue on days 2 and 3, actinomycin-D 0.5 mg on days 1 and 2, and then vincristine 1.0 mg/m^2 and cyclophosphamide 600 mg/m^2 on day 8). After two courses of chemotherapy, her serum β-hCG dropped to 36.7 mIU/mL. However, this increased to 94 mIU/mL at the end of the third cycle of chemotherapy, so she was referred to our institution. Our studies included brain, chest, abdominal, and pelvic computed tomography that revealed no evidence of metastatic lesions. Pelvic ultrasonography revealed a normal-sized uterus with no significant masses.

One cycle of chemotherapy consisting of PE (cisplatin 50 mg/m^2 on day 1, etoposide 100 mg/m^2 on days 1

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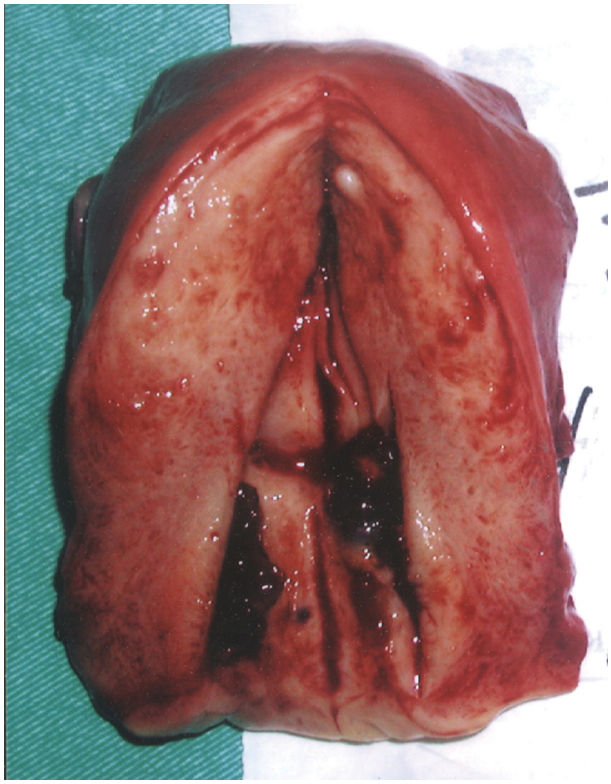

Figure 1. Gross specimen of the uterus. The tumor is located at the cervix.

and 2) was administered, and the β-hCG concentration decreased from 214 to 190 mIU/mL. At this time, the diagnosis was revised to PSTT because of the persistence of a low level of β-hCG that was refractory to EMA/CO treatment. The patient underwent total abdominal hysterectomy on July 10, 2003. The cut surface of her normal-sized uterus incidentally revealed a necrotic, soft mass measuring 0.8 × 0.5 × 0.5 cm in the endocervical wall (Figure 1). Grossly, the tumor had invaded nearly one-third of the thickness of the cervical myometrium. Microscopically, the tumor was composed of typical polygonal cells, most of which were mononucleate, but some of which were multinucleate (Figure 2). These findings were consistent with intermediate trophoblastic cells that had infiltrated the myometrium with fibrinoid pattern and presented in the central lumen of blood vessels. The tumor cells invaded the myometrium to a depth of 0.6 cm. Mitotic figure counts were four per 10 high-power fields. There was no villous formation. Most neoplastic cells stained with human placental lactogen (hPL) (Figure 3), whereas few stained with hCG (Figure 4). These histopathologic findings suggested the diagnosis of PSTT. After surgery, two cycles of EMA were administered, repeated at 8-day intervals. The patient's serum hCG dropped progressively to zero on August 7, 2003 (Figure 5). She was alive and well at the time of writing.

Discussion

PSTT was originally described by Kurman et al in a series of 12 patients, none of whom succumbed to their disease or had evidence of metastasis [1]. The term trophoblastic pseudotumor was used to reflect the clinically benign nature of this tumor. In 1981, Twiggs et al reported the death of a patient with trophoblastic pseudotumor due to distant metastasis [2]. Scully and Young then renamed the tumor placental site trophoblastic tumor to represent its malignant potential [3].

PSTT is a neoplasm composed of a monomorphic population of intermediate trophoblastic cells. Histologically, it is characterized by a mononuclear cell population that infiltrates the myometrium and its blood vessel walls. There is no dimorphic pattern of cytotrophoblasts and syncytiotrophoblasts. Villous formation is not present, while multinuclear giant cells are occasionally identified [4]. Generally, hemorrhage and necrosis, which are usually associated with choriocarcinoma, are not found. Immunohistochemical

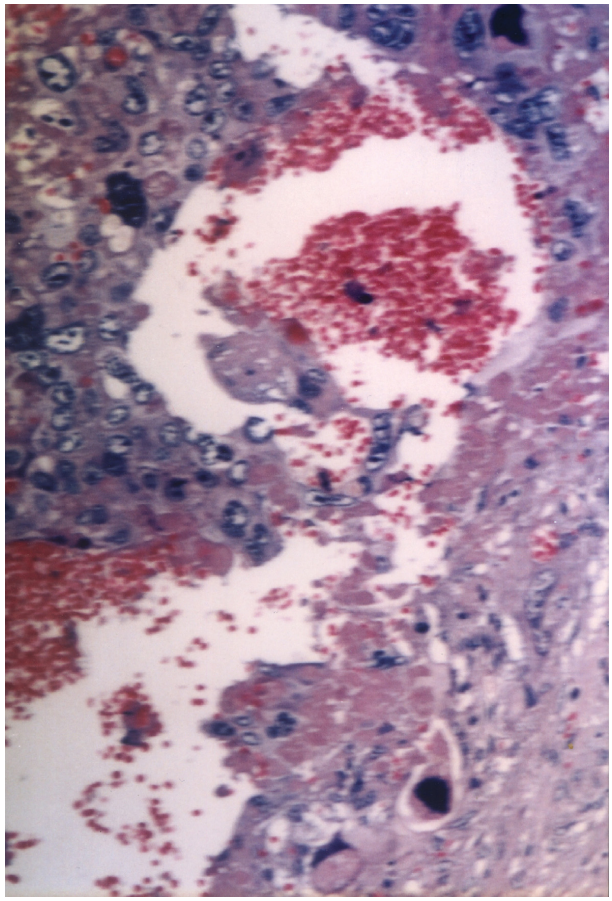

Figure 2. Photomicrograph of placental site trophoblastic tumor demonstrating a mononuclear cell population and occasional giant cells (hematoxylin & eosin, original magnification 20 × 10).

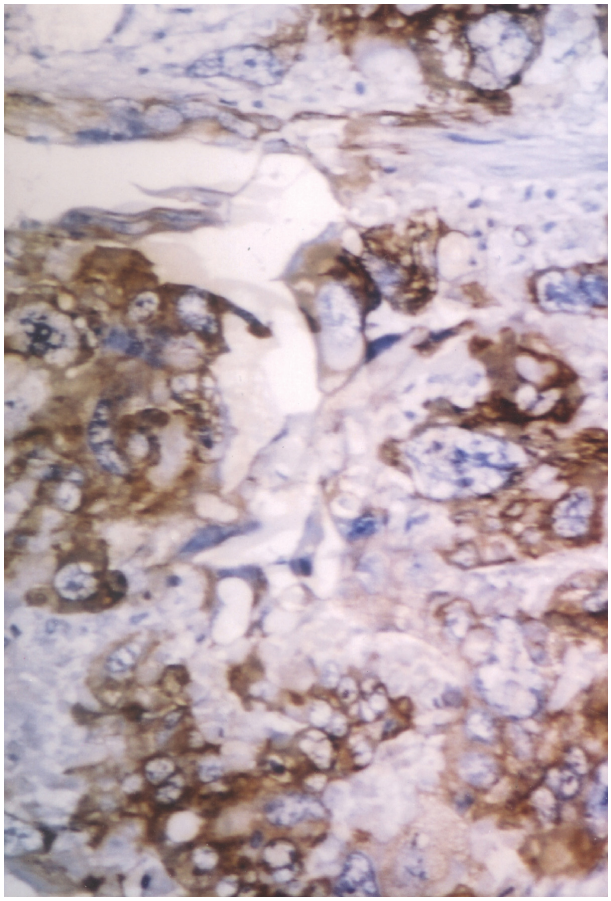

Figure 3. Human placental lactogen (hPL)-positive intermediate trophoblastic cells (hPL stain, original magnification 40 × 10).

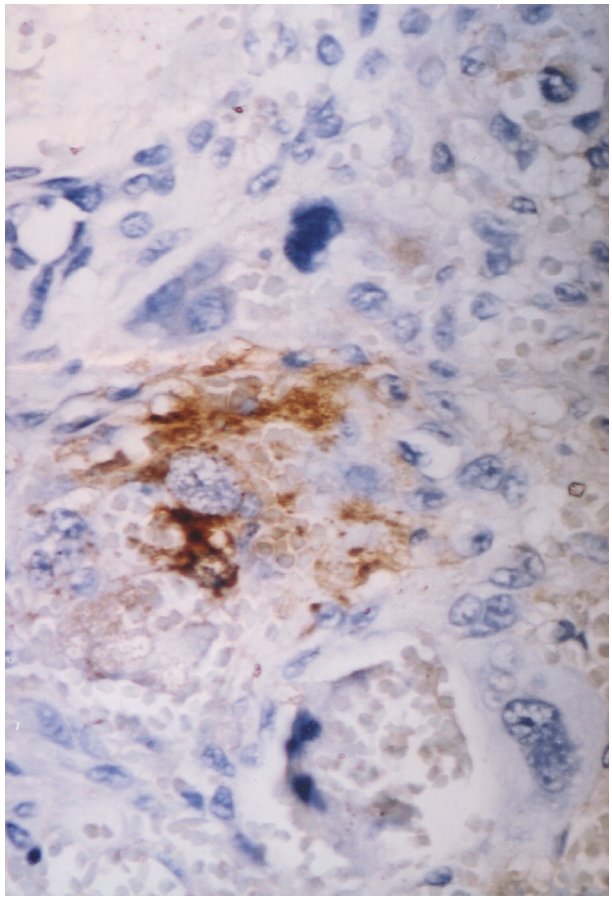

Figure 4. Human chorionic gonadotropin (hCG)-positive intermediate trophoblastic cells (hCG stain, original magnification 40 × 10).

staining is diffusely positive for serum hPL and only focally positive for hCG. hPL has been used as a tumor marker for gestational trophoblastic disease. Patients with PSTT may express low levels of hCG but have increased levels of hPL. However, we cannot measure serum hPL in our institution, so β-hCG was the only available tumor marker for this patient. The variable and often low level of hCG detected in this tumor reflects the lack of syncytiotrophoblasts.

Our patient met the diagnostic criteria for PSTT on the histopathologic findings from the resected uterus. The initial pathologic diagnosis was choriocarcinoma. According to a Japanese study, a correct diagnosis of PSTT is achieved in only 35% of cases on the basis of curettage specimens [5]. Vardar and Altintas showed that 50% to 100% of intermediate trophoblastic cells stain positive for hPL but less than 10% of tumor cells stain positive for hCG in patients with PSTT [6]. PSTT must be differentiated from choriocarcinoma and an exaggerated placental site. Compared with choriocarcinoma, PSTT has characteristic microscopic findings such as a monomorphic cell population, a pattern of immunohistochemical staining for hPL and occasionally hCG, and, usually, lack of necrosis and hemorrhage. PSTT can also be distinguished from an exaggerated placental site by lack of villous formation and occasional mitotic figures [7].

PSTT may complicate or follow any type of normal or abnormal pregnancy and affects women of all re-

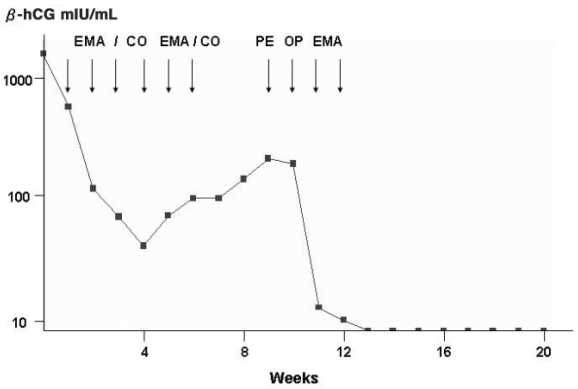

Figure 5. Serum human chorionic gonadotropin (hCG) level during therapy and follow-up. EMA = etoposide + methotrexate + actinomycin-D; CO = cyclophosphamide + vincristine; PE = cisplatin + etoposide; OP = operation.

productive ages. The most frequent gestational event reported is antecedent term delivery followed by spontaneous and therapeutic abortions [8]. Symptoms may develop from several weeks to up to 15 years after the preceding pregnancy [6]. Vaginal bleeding or amenorrhea is the usual mode of presentation. The antecedent pregnancy of our patient ended in therapeutic abortion. Nine months after the abortion, vaginal bleeding occurred. Ultrasonography usually shows an echogenic mass that may involve the endometrium and myometrium. The lesion was tiny after chemotherapy in this patient, so sonography failed to show the tumor.

Most PSTTs behave in a benign fashion, but approximately 10% to 15% are clinically malignant [9]. The tumors are usually non-metastatic and remain confined to the uterus. However, they can spread to the peritoneum, liver, pancreas, lungs, and brain late in their course and are usually not treatable in this setting as they do not respond to chemotherapy. Tumors with more than five mitoses per 10 high-power fields have an increased propensity for metastatic disease [8]. However, there have been several reports of recurrence developing with tumors with less than two mitotic figures per 10 high-power fields [10,11]. An interval of more than 2 years since the preceding pregnancy is an independent adverse prognostic factor [12]. Surgery remains the cornerstone of therapy, and primary total abdominal hysterectomy is the optimal therapy once the diagnosis of PSTT is established [12,13].

EMA/CO, an effective chemotherapeutic regimen, is the first-line treatment of choice for high-risk gestational trophoblastic tumors. Swisher and Drescher demonstrated that the total response rate to EMA/CO among metastatic PSTT was 71%, with a complete response rate of 28% [14]. Our present case initially responded to EMA/CO therapy but later became unresponsive. Chemotherapy-resistant persistent gestational trophoblastic disease may suggest PSTT [15]. A suggestion of PSTT may also arise from relatively low serum β-hCG concentrations [16]. For our patient, the diagnosis of PSTT was proved only by histopathologic findings from the surgical specimen. Hopkins et al suggest that the trophoblastic cells producing hCG are responsive to chemotherapeutic agents and that non-hCG producing trophoblasts are resistant [17]. It has been reported that failure of EMA/CO indicates that the tumor is aggressive [18]. Recently, Newlands et al used EMA/EP as the primary treatment for eight patients with metastatic PSTT, obtaining a 50% complete remission rate [19]. The clinical impression is that cisplatin should be included in the initial treatment of PSTT. We used one cycle of chemotherapy consisting of EP with some benefits before surgery. Adjuvant chemotherapy with two cycles of EMA was given, although the role of EMA has not yet been established.

To our knowledge, this is the first report of PSTT in the endocervical canal. The clinical behavior of endocervical PSTT is still unclear and there are no reliable prognostic indicators. It is also difficult to predict the clinical behavior of PSTT from serum hCG concentrations and the mitotic count in tumor cells. However, in general, this disease is highly curable if recognized and treated appropriately. Immediate hysterectomy is required for patients without metastasis until reliable prognostic indicators for PSTT are clearly understood.

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